New study strengthens link between everyday stress and obesity using an animal model

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Bethesda, MD-Stress can take a daily toll on us that has broad physical and psychological implications. Science has long documented the effect of extreme stress, such as war, injury or traumatic grief on humans. Typically, such situations cause victims to decrease their food intake and body weight. Recent studies, however, tend to suggest that social stress--public speaking, tests, job and relationship pressures--may have the opposite effect--over-eating and weight gain. With the rise of obesity rates, science has increasingly focused on its causes and effects--including stress.

A recent study conducted by the Departments of Psychiatry and Biomedical Engineering at the University of Cincinnati College of Medicine, examined the effects of stress on the meal patterns and food intake of animals exposed to the equivalent of everyday stress on humans. The results suggest that, not only does stress have an impact on us in the short term, it can cause metabolic changes in the longer term that contribute to obesity. The study was conducted by Susan J. Melhorn, Eric G. Krause, Karen A. Scott, Marie Mooney, Jeffrey D. Johnson, Stephen C. Woods and Randall R. Sakai at the University of Cincinnati College of Medicine, Cincinnati, OH. Their study was published in the American Journal of Physiology - *Regulatory, Integrative and Comparative Physiology*.

Previous studies have found that meal patterns (number, duration and size of meals) can affect metabolism. Studies of both humans and animals have shown that taking fewer and larger meals promotes the gain

of fat mass and can increase triglycerides, lipids and cholesterol independent of total caloric intake. Conversely, weight gain--even while overeating--can be prevented by consuming smaller, more frequent meals. Whether social stress alters the microstructure of food intake, however, was unclear.

The current study used the visible burrow system (VBS), an animal model of chronic social stress, which has been shown to produce stress-associated behavioral, endocrine, physiological and neurochemical changes in animals. Long-Evans rats (90 days old) were individually housed for three weeks prior to the experiment. During this habituation time, they were briefly anesthetized and implanted with a unique subcutaneous microchip just behind their ears which allowed for identification and monitoring of feeding behavior. Meal pattern characteristics were measured for seven days during habituation. Data were calculated for each animal for each day and then averaged together to provide an overall habituation measure as a baseline for all of the conditions.

For the experiment, rats were formed into colonies, composed of four males and two females, and matched with a control group. Within a few days, all colonies formed a hierarchy which established the dominance of one male and the subordination of the other three males. Each colony had equal hours of light and darkness. Meal pattern characteristics were calculated for each animal on a daily basis. As documented by behavioral video analysis and microchip data, both subordinate and dominant rats reduced their initial food intake and body weight compared to the habituation period and as compared to the control group. After the hierarchy was stable, however, the dominant rats recovered their food intake relative to the control animals, while the subordinate rats continued to eat less by reducing their number of meals. Furthermore, although rats are nocturnal animals, the subordinate rats ate primarily during lighted periods, indicating a shift in circadian

behavior.

After two weeks, the male rats were individually housed for a three-week recovery period and allowed to eat freely. Compared to the control group, both dominant and subordinate rats over- ate during the recovery period, but the dominant animals ate more frequently, while the subordinate animals ate larger meals, but less frequently. The dominant rats gained weight and lean mass, but only as comparable to the control group, while the subordinate rats gained significant fat in the visceral (belly) region. Throughout the recovery period, subordinate rats continued to overeat, eat longer meals and gain fat, suggesting long-term, deleterious metabolic changes.

Interestingly, the study results suggest that the signals controlling ingestive behavior become impaired or are overridden during social stress. Hypothalamic neuropeptide Y (NPY) is a well-known chemical messenger within the hypothalamus that stimulates food intake in times of negative energy balance, possibly by increasing meal size. In this case, NPY did not mediate the consumption patterns of the animals during the VBS period.

This is the first study of its kind to examine meal patterns in real-time during exposure to chronic social stress and during a subsequent recovery period, as well as to begin to evaluate the neuroendocrine and neurochemical underpinnings of the altered ingestive patterns observed. Stress and recovery induced changes in animals' body weight and composition and the alterations in meal patterns observed may have contributed to these physiological changes.

Stress is experienced by animals and humans on a daily basis and many individuals experience cycles of stress and recovery throughout the day. If, following stress, we consume larger and less frequent meals, the conditions are favorable for weight gain--especially in the abdomen. We

know that belly fat, as well as stress, contributes to the development of cardiovascular disease, immune dysfunction and other metabolic disorders. Further studies using the VBS model will help us understand the relationship between stress and obesity and help us treat and prevent the development of these diseases.

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